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EXAMINER

HM12/0716

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ART UNIT

PAPER NUMBER

1638

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/411,863

Applicant(s)

IZHAR, SHAMAY

Examiner

Anne Kubelik

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 June 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9 and 11-57 is/are pending in the application.
- 4a) Of the above claim(s) 1-9, 11-46, 48 and 52-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 47, 49-51 and 55-57 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

1. The cancellation of claim 10, the amendments to claims 47 and 49-55, and new claims 56-57 are entered. Claims 1-9 and 11-57 are pending. Claims 1-9, 11-46, 48, and 52-54 are withdrawn from consideration as being drawn to nonelected inventions. Claims 47, 49-51 and 55-57 are examined.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Amendment

3. Newly amended claims 52-54 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims are drawn to a plant **genome**, whereas the claims as originally written were drawn to a plant. If the claims as originally presented were drawn to a genome, they would have been restricted from the elected claims. The genome of claims 52-54 is a different chemical and physiological entity than the plants of the elected invention, and are thus unrelated. Additionally, the plants of the elected invention require methods of transformation and regeneration, not required by the genome of claims 52-54.

Since Applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 52-54 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

4. Claims 47 and 49 remain rejected and claims 56 and 57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, as stated in the prior Office action for claims 47 and 49.

Applicant's arguments filed 05 June, 2001, have been fully considered but they are not persuasive.

Applicant urges that the recombination problems described by Qin et al and Golic would not pose a problem for the instant invention, because they either would not occur or because progeny can be carefully selected to avoid plants that have these problems.

This is not found persuasive. Contrary to the assertions of Applicant the recombination events would not be minimized in the instant invention because the multiple site-specific recombination sequences (SSRSs) on each chromosome and the high rate of germline recombination in individuals homozygous for SSRSs, as discussed by Golic, would result in a large proportion of progeny having recombination between the SSRS on one side of the "third DNA segment" on one chromosome and the SSRS on the other side of that segment on the homologous chromosome, resulting in duplications of portions of the construct, rather than deletion. The evidence of Qin et al, while done with constructs on heterologous chromosomes, only emphasizes that interchromosomal occurs at high rates in plants and with the *cre-lox* recombination system. The instant specification does not teach how to avoid these problems.

As stated in the prior Office action, Lloyd et al teach that FLP/FRT recombination using a construct as described in the method of claim 47 did not work in *Arabidopsis* (pg 657, left column, paragraph 2: "Attempts to induce FLP/FRT recombination in the plant *Arabidopsis thaliana*, using the constructs described in this study, have so far failed"). The instant specification fails to teach the discovery of Luo et al (published in 2000) that in order to get the FLP/FRT recombination system to work in *Arabidopsis*, use of a FLP gene sequence with a variation in the sequence just upstream of the ATG initiation codon was required (paragraph spanning pg 427-428). Applicant urges that Luo et al states that another group of researchers teach FRT/FLP recombination in *Arabidopsis*. This is not persuasive because Luo et al also states that that the method requires an inducible heat-shock promoter. This promoter is not taught by the instant specification, which teaches a great variety of other promoters (pg 44 and Figs 1 and 2). Thus, unpredictability has not been overcome. As the method of claim 49 also reads on the use of the FLP/FRT recombination system (as illustrated in Figure 2), the unpredictability discussed here also applies to this claim.

Lastly, the claims are drawn to a method step of introducing a recombinase into a plant. The instant specification fails to provide guidance for application of a recombinase protein to a plant, getting the applied protein into the plant, and for having it reliably result in specific recombination.

5. Claim 50 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to a plant homozygous for an expression cassette that includes the following, in order: a first promoter, an SSRS, a second promoter operably linked to a first gene that activates the expression of the first promoter to direct expression of a second gene, another SSRS, and the second gene. The instant specification fails to provide guidance for selection of a first gene that can induce transcription through any transcription termination signals of the first gene to transcribe the second gene.

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate plant homozygous for the above described expression cassette.

6. Claims 50-51 and 55 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to plants with different exogenes in an allelic relationship. No description is provided as to the genotype or phenotype of the plants. Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed plants, one skilled in the art would not have been in possession of the genus claimed at the time this application was filed.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997), where it states:

The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's

relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA Accordingly, the specification does not provide a written description of the invention

7. Claims 47, 49-51 and 55-57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 47, 49-51 and 55 are indefinite in their recitation of the word “including.” It is unclear if this word is intended to be open or closed. If open language is intended, the word should be replaced with --comprising--. Note that claims 47 and 49-51 use the word in multiple locations in the claims.

Claim 50 is indefinite for having two periods, one at the end of the claim and one at the end of part (c).

The claims are indefinite for their confusing manner of describing the invention. For example, the expression cassette used in the method of claim 47, introduces three DNA segments, then says that the third segment is located between the first two; it would be more clear to described the DNA segments in order. Additionally, the multiple uses of “first” and “second” in the claim to modify “plant”, “segment”, “promoter sequence” and “transcribable polynucleotide sequence” adds to the confusion. The following changes would clarify claim 47 (similar amendments could be made to the other claims): 1. Instead of talking about a “first plant” and a “second plant”, which are identical, it would more clear to refer to backcrossing the plant resulting from step (b) to the original plant. 2. The expression cassette should be described with each component in order, i.e., a first promoter, an SSRS, a second promoter operably linked

to a first gene, another copy of the SSRS, and a second gene. Wording of all amendments require support in the specification.

Claim 47 is indefinite for its recitation of "isogenic plants for an expression cassette". Plants can be isogenic for an expression cassette, but the current wording makes it appear that the plants are to be used as an expression cassette.

Claim 49 has a lack of agreement in plurals in the phrase "a first and second plants".

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

9. Claim 55 is rejected under 35 U.S.C. 102(b) as being anticipated by Vergunst et al, as stated in the prior Office action for claims 10, 52 and 55.

Applicant's arguments filed 05 June, 2001, have been fully considered but they are not persuasive.

Applicant asserts that the plants generated by Vergunst et al have the *bar* gene expressed from both chromosomes, and as such segregation of this exogene will not occur in the gametes.

This is not found persuasive. The plants of Vergunst et al are homozygous for the *bar* gene and hemizygous for the *np1II* gene. This is exactly analogous to the plants of Figure 1, which are homozygous for the T7 Polymerase gene and hemizygous for the Toxin gene. As

Applicant considers the plants of Figure 1 to exhibit true exogenic allelism, the presence of the bar gene on both chromosomes in the plants of Vergunst et al is irrelevant. Note that the definition of “exogenic allelism” in the instant specification is the “allelic positioning of two functionally distinct exogenes on the chromosomes of a chromosome pair such that substantially 100% segregation of the two exogenes is observed upon gamete formation” (paragraph spanning pg 26-27), and the definition of exogenes is “polynucleotide sequences which are trans-introduced and integrated in a genome of a species” (pg 27, lines 3-5). Whether or not the gene is expressed is not a component of the definition.

Additionally, Applicant urges that the constant expression of a recombinase in the plants will lead to nonspecific recombination and less than optimal segregation of the two exogenes within the gametes; thus segregation of the exogenes cannot be predicted with certainty.

This is not found persuasive. The plants of Vergunst et al showed segregation with a χ^2 test for goodness of fit yielding $P > 0.05$ (pg 2732, right column, paragraph 1). Thus, the conditions of segregation and the definition of exogenic allelism have been met by the plants of Vergunst et al.

10. Claim 55 is rejected under 35 U.S.C. 102(b) as being anticipated by Fabijanski et al, as stated in the prior Office action for claims 10 and 52-55.

Applicant's arguments filed 05 June, 2001, have been fully considered but they are not persuasive.

Applicant asserts that Fabijanski et al do not teach methods of generating plants that exhibit true exogenic allelism, in that they would obligatorily segregate the two genes into different gametes.

This is not found persuasive. The method of claim 9 of the issued patent would produce plants that exhibit true exogenic allelism because the genes segregate during meiosis.

Claim Rejections - 35 USC § 103

11. Claim 51 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lloyd et al in view of Snaith et al.

The claims are drawn to plants homozygous for an expression cassette that includes two genes and two different sets of SSRs.

Lloyd et al teach plants with SSR-containing constructs (Fig 1 and 2) and suggest expressing two different site-specific recombination systems in the same plant (pg 653, right column, 1st full paragraph). Lloyd et al do not teach plasmids with multiple different SSRs.

Snaith et al teach plasmids with multiple FRT and *loxP* sites, suggest their use in combined manipulation strategies, and discuss their importance as tools in *in vivo* manipulation of DNA (Fig 1 and pg 173, right column, and abstract).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to produce plants with SSR-containing constructs as taught by Lloyd et al, and to modify that to use constructs with two genes and two different sets of SSRs as described in Snaith et al. One of ordinary skill in the art would have been motivated to do so because of the suggestion of Lloyd et al to use more than one site-specific recombination system in the same plant (pg 653, right column, 1st full paragraph).

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12. Claims 47, 49-50 and 56-57 are free of the prior art, given the failure of the prior art to teach a method of backcrossing plants produced by a recombination system, given the unpredictability inherent in using these recombination systems in *Arabidopsis* and in plants homozygous for SSRS-containing constructs, and given the unpredictability of the transcriptional read-through required for the plant of claim 50.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached on Monday through Friday, 8:15 am - 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula K. Hutzell, can be reached on (703) 308-4310. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.
July 12, 2001

DAVID T. FOX
PRIMARY EXAMINER
GROUP ~~100~~ 1638

David T. Fox